

1 April 1999

Trip report: Paris (18-19 March), IPSN Technical Steering Committee
Minsk (22-23 March), BelAm Thyroid Project
Kyiv (24-26 March), UkrAm Thyroid Project, Leukemia Project, STCU

PARIS

Institute of Nuclear Safety and Protection

The first stop on this tri-national trip was Paris, visit to our French collaborators from the Institute of Nuclear Safety and Protection. The meeting was held in the facilities of the Atomic Energy Commission in center Paris with the following in attendance: American side: Drs. Finch, Howe, Bouville and myself and the French representatives: Drs. M. Tirmarche, D. Thierry, M. Adam (the pathologist that participated in the diagnostic review program in Kyiv), M. Valente and P. Verger. Drs. P. Hubert and P. Gourmelon joined us on the second day.

Dr. Tirmarche expressed their interest in working much closer during the second phase when it gets underway. They would like to go frequently to Ukraine and possibly they could even come with additional funds for supplies/equipment.

I discussed recent developments at the NCI, the formation and relocation of the Chernobyl Research Unit, our intent and the reasons for extending Phase I by six months and preparatory work which should precede the decision making on possible implementation of Phase II. Then I summarized the expenditure of French funds for supplies and equipment and NCI director's commitment to this project and increased financial support, the role of Columbia contract and formation of various reviewing and oversight groups on our side.

Dr. Finch reported on the hematologic review held in January in Kyiv with the goal of evaluating the original diagnoses made in various hospitals in our area of interest and exploring the level of expertise in Ukraine. The five members of the review team included Drs. Preston and Reis (from the USA), Dr. Adam (from France) and Drs. Gluzman and Haydukova (from Ukraine). There were some difficulties encountered in obtaining the pathological materials from different oblasts (Sumy lost most of their material during a fire, Donetsk due to flood), in many places the slides are kept only for a year or two and then washed and reused; also, some pathologists were very uneasy in parting with their slides. However, in the end 115 cases were available for this review: 80 leukemia and 15 lymphomas plus an assortment of other hematologic cases. These were retrospective cases obtained from general population. In setting it up we assumed that the handling of liquidators should have been at least as good as that of general population or better. In the future, Dr. Finch felt that we should be prepared to remunerate the local workers searching for such material in their files.

Dr. Adam noted that he was somewhat disappointed in then limited number of different diagnoses; most of the available cases were easy to diagnose, he thought. But, overall, the participating reviewers agreed remarkably well with the original diagnoses and among themselves.

Dr. Howe explained his view of this project. We were supposed to identify a cohort of liquidators in six oblasts: Kyiv, Chernyiv, Luhansk, Donetsk Dnipropetrovsk and Kharkiv. During the last year it appeared that some of these oblasts would not be able to provide the necessary material for the study, so Luhansk and Donetsk were replaced by Cherkasy and Poltava. Dosimetry is very important in this work. If we will not be able to attain our projected cohort level, we could switch to a case control or case cohort design. To provide a satisfactory uniform dose for these cases, the soft expert assessment dose (SEAD) was developed by Dr. Kryuchkov from Moscow and it should be evaluated shortly on a group of liquidators. He noted that State Registry of Liquidators is not as accurate as the Oblast Registries which provide about 20% more entries than State.

Dr. Pierre Verger then reviewed the German-French effort in Chornobyl related studies: the problems related to the sarcophagus, radio ecologic studies and health consequences of the Chornobyl Accident. Dr. Tirmarche expressed an interest in the work of USAIA team (Dr. Contis) in Ukraine. She worried about the overlap with our thyroid project.

Next day I had to take Dr. Howe to the Ukrainian Embassy to get him a visa for Ukraine which we were not able to get in the States because his passport was kept too long at the Belarusian Embassy. We missed a portion of Dr. Hubert's presentation of the IPSN organizational schema which was requested by Dr. Finch.

Returning to our concerns, Dr. Tirmarche noted that selection of various sites for subject sources should be made on the basis of the available numbers from the Registry rather than because of the ease of work, distance or internal politics.

Dr. Bouville reported on his work: inventory of the available doses (Chornobyl Registry), development and implementation of new dosimetry methods and inter-comparison of different methods. It was brought out that the Kryuchkov method should be tested on Ukrainian liquidators and compared with EPR measurements and that it will have to be paid for because the interviewers and the analysts to be used are not at this time members of the pilot project staff. The doses obtained from these calculations will be calibrated using bio- and physical dosimetry, although there is some doubt whether the FISH test will be sufficiently sensitive in the lower dose range.

Dr. Tirmarche would like to have us develop a schedule of events for the entire 1999 so that proper plans could be made by everybody. In the past they have had some difficulties to join us on our visits because of conflicting commitments.

Dr. Hubert noted that there are many papers on dose distribution. It is about time to synthesize some conclusions from them.

I presented a rough sketch of events for the next nine months. Presently the most important task is to get Dr. Chumak started in his work on EPR. His new instrument should be operational in late April, I found out later in Kyiv. Dr. Kryuchkov's method needs evaluation. In September-October time frame we should expect a draft report of the progress in Phase I which will serve as a preliminary indication of whether Phase II will be possible. It will be critically reviewed by NCI and IPSN. If positive, we will concentrate on a proposal for Phase II and in any case will prepare an exhaustive terminal report. I expect a plenary session in June (21-24) and then in early October for these events. The issue remains how to integrate the French colleagues in this work, how to resolve the issue of ancillary studies that may arise in

epidemiology, dosimetry, hematology, etc. Finally, a new Protocol for Phase II will have to be developed.

MINSK

Clinical Research Institute of Radiation Medicine and Endocrinology

On Monday morning we met in the new dispensary facilities. Except for the main corridor where work continued on air ducts and installation of the ceiling and finishing touches in the registration room, the other rooms were already occupied and busy or ready for occupancy (the laboratory was supposed to have moved into their new space toward the end of the week). The rooms are organized according to the flow of screenees: registration-interview-data entry-clinical examination-ultrasound-laboratory. Dr. Rzhetskiy's office is in a different wing but easily accessible. The dosimetrists are in a different location which I have not seen so far. The epidemiologists and DCC personnel were in the process of moving to their new facilities approximately half way between the dispensary and the old location on the Masheroova street. This facility will need a lot of work and some financial commitment to provide adequate working conditions. Presently it is a huge open space measuring 36 by 55 feet, three sides of which have floor to ceiling windows with south to south-west exposure; this space is on 11th floor so there is no protection from the sun. In summer it will cause problems with our computers. Walls are not permitted to be put up so high noise level is to be expected. At present they are attempting to separate this huge area into six modules using their furniture (book cases, filing cabinets). Drs. Polanskaya and Lesnikova were obviously not happy with this location; they would prefer the dispensary site. In later discussion with Dr. Rzhetskiy he mentioned that there may be more space generated in the dispensary, so there is hope, I think.

The first item of business with Dr. Rzhetskiy was a request for additional filing cabinets. They were not happy with the ones we bought them because "it was difficult to locate individual files". I discovered that the reason for it was that these were cabinets for hanging files and nobody explained it to them that what they need are hanging folders. I tried to explain it but I am not sure that I sold them on it. They have an established way of storing their clinical records and they want to continue using these bookshelf-like cabinets.

On the subject of mobile team activity they began to experiment with the method used in Ukraine, i.e. bussing the cohort members to Minsk for examination rather than relying only on the mobile teams set out to the countryside. People believe that in Minsk, or in Kyiv, the facilities and the staff are much better than in their local dispensaries and, whereas they would not consent to participate in local screening effort, they would go gladly to Minsk if transportation were to be provided. The last point is the deciding factor, because in the past the difficulty in reaching Minsk from remote areas was the reason given for non-participation. I was not surprised that they immediately asked for a bus to be provided by us for this activity.

Dr. Rzhetskiy has obtained from Project HOPE some multivitamins and chocolate bars. The mobile teams started distributing them to the screening candidates and evidently this was well received. He made a pitch for getting some gifts to be used as an incentive to the participants. Several items were suggested: baseball caps, T-shirts with our logo, pens, but not money. The opinion on food items was mixed; politically it could be incorrect.

Dr. Polanskaya was busy reviewing and checking the records produced in the screening process and found some discrepancies which resulted in removal of some cohort cases. Her efforts in introducing practical quality control measures begins to pay off.

The principal reason for my trip was to meet with Belarusian component of the Binational Advisory Group. A meeting was set up for the afternoon. During the morning discussions with Dr. Stezhko it became obvious that they "missed the boat". What they had was the local IRB, or as they call it "ethical committee" scheduled for our afternoon session. After some digging I found out that the list of names that we received for the Binational Committee was never seen by Dr. Stezhko and nobody seemed to know about it. One of the members of that list was actually dead now. It was too late to change the meeting at this stage so I agreed to meet with them and explain what a Binational Advisory Group is and our view of their role and activities as well as the need for representatives of the various disciplines involved in the project.

Four individuals showed up for the meeting: Igor Grigorievich Zhakov, chairman, radiation oncologist; Ivan Osypovich Goncharek, internist; Nona Grigorievna Rys, pediatrician; and substituting for Dr. Lipski Lidia Nokolayevna Litvinovich a lawyer from Belarusian Children's Fund. They listened attentively to my presentation but only Dr. Zhakov, who incidentally did spend some time in the USA at SKI and M. D. Anderson, realized immediately that they do not belong on such a committee. Later, Dr. Stezhko agreed that he has to restructure their group membership. He will retain Dr. Zhakov as the chairman and pick other candidates in line with the requirements. I should be getting his new list soon.

The second day I spent in the dispensary. The recurring topic was the establishment of a branch in Gomel. Dr. Rzhetskiy insisted that an additional mobile team would be adequate to increase the numbers. His plan was based on one stationary team in Minsk with three mobile teams of which two would be working in the country and one would provide the second shift in Minsk (they work from 8 AM to 6 PM). This would provide a "rest period" every other week from being away from their homes. Again the need was stressed for a bus to bring people to Minsk. They were strongly against a second center for the study. However, when this topic was raised again later in the day with Dr. Ostapenko, the new Director of the Institute and Deputy Project Director for Science, the mood changed. There would be only one official center in Minsk, but a Mobile Team Branch would be set up in Gomel. Dr. Ostapenko said he was going to Gomel next day and he will discuss this with the staff of Gomel Branch of the Institute. He was sure that he could get the ultrasound equipment for it and Dr. Rzhetskiy was willing to train the members of the mobile team and certify them officially. Obviously this needs to be watched, but I believe that Dr. Ostapenko will be successful in establishing the Gomel Branch.

I discussed current need for supplies and equipment with each group and new lists were submitted. Besides some of the already mentioned items, more computers are needed and transportation for the dosimetrists to do their interviewing. We decided to try at first renting the vehicle as needed rather than purchasing one. It may be less expensive in the long run (driver, gas and maintenance is provided on rental contracts). The most dire need appears to be the vacutainers which, unfortunately are not available locally so must be imported. The order for hormonal assays has been placed with BRAHMS, as we had very bad experience with Abbott, and BRAHMS could provide luminescent test kits which have much longer life span than RIA reagents and which would provide the same systems in Belarus and Ukraine. Early in April a

workshop will be held by BRAHMS staff in Gomel and I suggested that Dr. Petrenko attend that session. Dr. Stezhko agreed to it.

Drs Buglova and Polanskaya would like to get some training in the U.S. and Dr. Zhakov wondered if he could possibly attend a meeting of our IRB sometime to learn how we are doing it. Everybody was asking when Dr. Mincey will come again to work with them.

I raised the issue of multiple entry visas again and asked to be copied the correspondence between their Ministry of Foreign Affairs the Belarusian Consulate in Washington. We are having difficulties with getting multiple entry visas for our non-government participants (only three of us from NCI have multiple entry visas for one year only). I hope this will be somehow resolved.

I discussed with Dr. Stezhko the possibility of the BelAm project becoming a partner with International Science and Technology Center (analogously to the UkrAm projects being partners with Science and Technology Center of Ukraine) for the purpose of allowing a simple and reliable route of delivering funds for the local support and even purchasing items available on local markets rather than importing them every time they are needed. Evidently the initiating point for this to happen is a letter from our Dpt. of State and I will have to contact Mr. Noble to urge him to do it.

Next morning I took one of the last flights by Belavia Airline with direct connection to Kyiv. From now we will have to go via Warsaw or Frankfurt to get from Minsk to Kyiv.

KYIV

Institute of Endocrinology and Metabolism

Immediately upon my arrival from Minsk, I went to the Institute to meet with the Ukrainian component of the Binational Advisory Group. In contrast to the Belarusian situation, the project director, Dr. Tronko, was in contact with the established committee and I believe they have even met at least once before. The committee was established 13 August 1997 by a Ministerial order No. 2522/42. Unfortunately we have never seen this document, and as far as I know it only exists in Ukrainian language. I have received a copy now. The committee members are:

Ukrainian Chairman: Dr. V. V. Frolkis, Deputy President of the Ukrainian Academy of Medical Sciences, radiation biologist;

Members: Dr. I. R. Barylak, Director of the Ukrainian Scientific Hygiene Center, Radiation dosimetrist;

Dr. P. M. Bodnar, Department Chairman of Kyiv Medical School, endocrinologist;

Dr. O. V. Korkushko, Department Chairman at the Institute of Gerontology, pathologist;

Dr. E. G. Pedachenko, Chairman of Scientific Medical Council, Ministry of Health, radiation epidemiologist.

Dr. Tronko gave the progress report on all activities in this project and discussed the proposed

changes to the protocol. I followed by a report of our meeting with the American component of the Binational Advisory Group and our concept of the operation of this Group. The one problem which surfaced was that the originally proposed dates for the meeting on 13-14 May were now not acceptable to Dr. Tronko and his staff due to some conflict. I agreed to try to change this date but could not promise it because we were pretty much locked to this week. Incidentally, upon my return I found out that some of our members are already committed for the week following the proposed dates. I am now communicating this to Dr. Tronko.

Thursday morning I visited the newly appointed First Deputy of the Minister of Health for the Chernobyl Projects, Dr. Olga Bobyliova. In the past she was a staunch supporter of our project and met with us often during our visits. She assured me of her strong interest and that she will do her best to assist the project staff in fulfillment of their tasks.

The rest of the morning was spent in trying to reach the new staffer in the U. S. Embassy who replaced Mr. Doug Apostol with whom we had longstanding relations. The man in charge of Chernobyl activities now is Mr. Bruce Hudspeth (Tel: 244 7345). I was only able to reach him by the phone. My principal concern was the renewal of the U.S.-Ukraine agreement on continuation of our collaboration. He told me that Ms. Kessler (DoS) was in Kyiv recently attending a conference on this matter. It was decided that the first step will be an exchange of diplomatic note (dip-notes) stating our intent to continue the work. This will be followed by an official memorandum the text of which is presently being staffed. He expressed his interest and the need to learn more about our project, but at this time he was unable to see me.

In the afternoon I had another session with Drs. Tronko and Tereshchenko. I reminded them that we are due for renewals of the IRB clearance, the extension of the STCU agreement and the quarterly progress report. I reminded them that their IRB committee should have a meeting as well and the minutes must be submitted with our documentation. I requested for a short bio-like description of the professional background of their Binational Advisory Group members and asked Dr. Tronko for the hard copies of his slides that he used in his presentation. In turn, I gave them the material on our members and our proposals for changes in the protocol. We agreed to coordinate our work with theirs and present one document for review and approval by the advisory group in May.

Additionally we discussed the need to determine the reasons for such a high non-compliance rate among the cohort candidates. I was told that they already started working on it by requesting the people that decided not to participate to state their reason for this. I will be looking for their report.

Currently the USAID is sponsoring a screening program for thyroid abnormalities among school age children in Ukraine. We were concerned that they may cross with our cohort members and that we should agree to share data in such cases so as to avoid double examinations. Dr. Tronko felt that there is little likelihood that our path may cross. They started in westernmost Ukraine and will slowly move east. By the time they reach Kyiv oblast, our cohort will be over 14 years old and, even if they might catch isolated individuals, the incidence should be minimal. But he agreed that in such cases there will be full cooperation.

Science and Technology Center of Ukraine

Several concerns expressed by our project colleagues prompted me to call on the STCU staff. Unfortunately Dr. DuCharme, the executive director, was in the States so I could discuss the apparent problems only with the coordinator of our partnership, Mr. P. Motovkin and the Ukrainian executive director Dr. Otamanenko.

Some of these "problems" were just misunderstandings, some expressed undue worry about the processing of funds in light of the banking crises that swept Russian and Ukraine, some were due to delay caused by the participants themselves (no bank account, no invoice, etc.). As noted, this started when the bank used by STCU went bankrupt. None of our money was lost, STCU covered the losses and found another bank. Our colleagues can use it or can find their own bank. This too led to a misunderstanding in that it was felt that STCU tries to shift the responsibility for the banking away from themselves and put the burden either on the projects or even on their staff. Because the money trading was officially closed by the government during the Hryvnia stabilization period, only commercial exchanges were permitted and they took longer than usual. Because of it the money availability was delayed by a week or so. Mr. Motovkin suggested that if anybody needs to talk to STCU staff, they should always ask for him and their financial officer to make sure that there are no crossed signals.

Next I raised the question of the six months extension of leukemia project; all we need to do is send them an official request and this will be handled as an extension of the on-going arrangement. However, the annual renewal of the thyroid partnership should be initiated soon. While preparing this document we could add the purchasing of local goods for our project. STCU would handle this easily enough and recently they have received the authority to clear incoming items through the customs. This appears to be a workable solution and would relieve the Columbia contractor from multiple small purchases on local economy.

Research Center for Radiation Medicine

I met with Drs. Romanenko and Bazyka Friday 26 March in their Melnikova street center. Dr. Romanenko is preparing for the opening of his new Medical Center in Sviatoshyn and, as expected with new construction, not everything is as ready as it should be so he is working under considerable stress.

His first concern was about the extension of the project for six months so that the work in dosimetry could be completed. The required instruments have arrived just recently and are just being set up. I explained that we are working on this and the required sum and the time extension will be handled in time. A related question concerned possible extension of the pilot work to a full study. I stated that during these next six month all the preparatory work needs to be completed. Then a careful analysis of the results should be prepared on the basis of which a go-no-go decision will be made. This should occur around September-October. If the decision is to proceed, this will give them adequate time to prepare a planning phase, to minimize time lost between the two phases. Then finally, the detailed proposal for the phase two could be made.

Another burning issue is the extension of the U.S-Ukraine agreement on cooperation on the effects of Chornobyl accident on leukemia among the liquidators. The National Agency of Ukraine for Development and European Integration which is responsible for registering projects

which are relieved from import taxation and duties is concerned that the original agreement lapsed last December. Without a continuation agreement our tax free status would lapse as well. They were cooperating with us thus far, but now they need the necessary documentation. I told them about my conversation with Mr. Hudspeth and the steps that our Department of State is about to undertake. We have urged them to process these documents and now we have to wait for their reaction.

The next problem was raised by Dr. Bazyka who is trying to get their FAC scan machine repaired. This instrument will be needed in the hematology work and it is less expensive to repair an existing unit than to buy a new one. Originally we were told that at a slightly higher cost we could get a one year maintenance service which would take care of any problems during the next year. Now, Dr. Bazyka presented me with cost estimates and they are not "slightly more". I told them that I need to discuss it with our staff and consultants to decide what is most cost efficient and necessary for our work.

The next instrumentation problem concerned the EPR equipment for Dr. Chumak. The equipment arrived with some small parts missing (mostly cables). To ship these parts directly will most probably get them stranded in the customs office. And time is of essence, so it was proposed to bring the company's technical representative to Kyiv who could deliver these parts, set up the instrument and certify its performance. A written cost estimates was received. I am inclined to approve this because this will be the speediest way of handling it and will extend the warranty for this instrument which should cover the "dead" time lost thus far in the process of ordering, delivery and customs clearance.

We discussed the dates for the June plenary program review meeting (21-24 June). Time permitting, a visit to Cherkasy (the new center proposed by Dr. Romanenko which is to replace the Luhansk center) could be arranged.

Before coming to Kyiv, I have heard from Drs. Bouville and Howe that Dr. Kryuchkov's method for calculating doses received by the liquidators should be validated by field study performed on 50 volunteers from Ukrainian liquidators and after some adjustments verified on an additional sample of 50 liquidators. Presently I received a cost estimate for this work from Dr. Chumak. Unfortunately, Dr. Romanenko has not seen it and I needed his approval before authorizing this expense. Dr. Romanenko agreed and will send me an official letter concerning this.

The final topic concerned training of one of Dr. Pilinska staff; I was working on it now for six months or so and we were not able to find time suitable to the candidate and to the laboratory where the training is to take place. I suggested that we reactivate this during this coming summer when the workload will be somewhat diminished.

Ihor J. Masnyk
Project Director